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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/501,689 | 07/17/2004 | Chengzhi Zhang | 5108N1P1 | 4379 |

35969 7590 10/26/2006

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|---|---|
| SOLOLA, TAOFIQ A | |
| ART UNIT | PAPER NUMBER |
| 1626 | |

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/501,689 | ZHANG ET AL. | |
| | Examiner | Art Unit | |
| | Taofiq A. Solola | 1626 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-6,8-12 and 14-26* is/are rejected.

7)☐ Claim(s) *7 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-26 are pending in this application.

## Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-26, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims lack adequate support in the specification. The claims are drawn to method of treating or preventing proliferative disorders. The specification fails to provide conclusive evidence that the instant compounds could be used for treating or prevent any solid tumor or proliferative disorders. Applicant's reliance on testing lung carcinoma cells is misplaced because is not evidence that all forms of cancers are treatable and/or preventable.

Claims 22-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for using the instant compounds for the treatment and/or prevention of any solid tumor or all proliferative disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

"'In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, It is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the [compounds and the utilities]

as obviously correct." *In re Jolles*, 628 F.2d 1327, 1332 (Fed. Cir. 1980), citing *In re Novak*, 306 F.2d 924 (CCPA 1962); see 340 F.2d 974, 977-78 (CCPA 1965).

"A specification disclosure which contains a teaching of the manner and process of making and using the invention . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), Id. at 1566, quoting *Marzocchi*, 439 F.2d 220, 223 (CCPA 1971); *Fiers v. Revel,* 984 F.2d 1164, 1171-72 (Fed. Cir. 1993), quoting *Marzocchi*, 439 F.2d at 223; see also *Armbruster*, 512 F.2d 676, 677 (CCPA 1975); *Knowlton*, 500 F.2d 566, 571 (CCPA 1974); *Bowen*, 492 F.2d 859 (CCPA 1974); *Hawkins*, 486 F.2d 569, 576 (CCPA 1973).

Where there is "no indication that one skilled in the art would accept without question [the instant compounds and method of use] and no evidence has been presented to demonstrate that the claimed products do have those effects *Novak*, 306 F.2d at 928, an applicant has failed to sufficiently demonstrate sufficient utility and therefore cannot establish enablement."' *In re Rasmusson,* 75 USPQ2d 1297 (CAFC 2005). The claimed utility is not enable without undue experimentation for the following reasons:

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered. *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC, 1988):

"The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218

(1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. The specification states:

> **The utility of the compounds of the present invention can be illustrated, for example, by their activity *in vitro* in the *in vitro* tumor cell proliferation assay described below. The link between activity in tumor cell proliferation assays *in vitro* and anti-tumor activity in the clinical setting has been very well established in the art. For example, the therapeutic utility of taxol (Silvestrini et al. *Stem Cells* 1993, 11(6), 528-35), taxotere (Bissery et al. *Anti Cancer Drugs* 1995, 6(3), 339), and topoisomerase inhibitors (Edelman et al. *Cancer Chemother. Pharmacol.* 1996, 37(5), 385-93) were demonstrated with the use of *in vitro* tumor proliferation assays.**

The above statement relates to taxol and taxotere, which are known to disrupt microtubules in cells and therefore very toxic but effective against various forms of cancers. Also, the instant compounds do not share structural similarity with taxol or taxotere, and are not disclosed in the specification as topoisomerase inhibitors. Therefore, the statement cannot be the basis of support for the instantly claimed utility.

On page 125, lines 19-22, the specification defined hyperproliferative disorders by examples. However, "[e]xemplification is not an explicit definition." The specification must set forth the definition explicitly and clearly, with reasonable clarity, deliberateness and precision, *Teleflex Inc. v. Ficosa North Am Corp.*, 63 USPQ2d 1374, (Fed. Cir. 2002), *Rexnord Corp. v. Laitram Corp.*, 60 USPQ2d 1854 (Fed. Cir. 2001). The disclosed examples include cancers. There is no evidence that the instant compounds would treat and/or prevent all categories of tumors or cancers namely: carcinoma, sarcoma myeloma, leukemia, lymphoma and mixed types. Only the testing of lung carcinoma cells (H460) is described in the specification.

The "fact that [the] art of cancer chemotherapy is highly unpredictable places on drug patent applicants to provide basis for believing speculative statements placed in the

specification as positive assertion are true, and failing such, ignorance of PTO in not being able to provide scientific reason why assertion is not sound is not justification for permitting assertion to be made, where those of ordinary skill in the art would not accept assertions as believable without some data or other evidence to support it." *In re Hozumi,* 226 USPQ 353, (ComrPats, 1985). "Proof of utility is sufficient if it is convincing to one [of] ordinary skill in the art, amount of evidence required depends on facts of each individual case, character and amount of evidence needed may vary, depending on whether alleged utility appears to accord with or to contravene scientific principles and beliefs." *In re Jolles,* 206 USPQ 885 (CCPA, 1980).

"[W]here application is directed toward treatment of humans, clinical case histories showing that compound is useful in the treatment of two types of cancer (in the instant case one type), do not establish utility of compounds for treatment of other kinds of cancers, such evidence, limited to one compound and types of cancers, is not commensurate with [a] broad scope of utility" of treating all forms of cancers. *In re Buting,* 163 USPQ 689 (CCPA, 1969). Even though "the state of cancer treatment has advanced remarkably, decisional law would seem to indicate that the [instantly claimed] utility is sufficiently unusual to justify an examiner's requiring substantial evidence, which may be in the form of animal tests." *Ex parte Krepelka, et al.,* 231 USPQ 746 (BdPatApp&Int, 1986).

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding any of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. The purpose of 35 USC 112 is to obviate the need for this type of experimentation. *In re Borkowski,* 164 USPQ

642 (CCPA,1970). See also, *Univ. of Rochester v. G.D.Searle & Co,* 68 USPQ2d 1424 (DC WNY, 2003). By limiting the claims to treating lung cancer the rejection would be overcome.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-6, 8-9, 14-18, 20, 22-23, 25-26, are rejected under 35 U.S.C. 102(b) as being anticipated by Braunlich et al., EP 779291 (US equivalent 5,922,740).

Braunlich et al., disclose compounds in Table 1 (minus XVIII, XXV, XXVII-XXIX), their compositions and method of use for treating various proliferative disorders. See the table, the abstract and column 9, second paragraph of US '740.

Claims 1-2, 4-6, 8-9, 14-18, 20, 22-23, 25-26, are rejected under 35 U.S.C. 102(b) as being anticipated by Braunlich et al., EP 0 731 099 B1.

Braunlich et al., disclose compounds III-IV, VIII, XI-XIII, XXVI, XXVIII-XXXIII, XXXV-XLVIII, LI-LII, LVI-LVII, LXV-LXVII, LXIX, their compositions and method of use for treating various proliferative disorders. See Tables I-V, and paragraphs 0028 and 0029 on page 10.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 11, 14, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over McKinnon et al., Canadian J. Chem., (1984), Vol. 62(8), pg. 1580-1584, and Boeshagen et al., Justus Liebigs Annalen der Chemie., (1972), Vol. 764, pg. 58-68, individually.

Claims 1-2, 4-6, 8-9, 16, are rejected under 35 U.S.C. 103(a) as being unpatentable over Harwalkar et al., Indian J. Het. Chem., (1994), Vol. 3(4), pg. 247-52, and Osswald et al., EP 755934, individually.

Claims 1-6, 8-12, 14-21, are rejected under 35 U.S.C. 103(a) as being unpatentable over Radl et al., Collection of Czechoslovak Chem. Commu., (2000), Vol. 65(7), pg. 1093-1108.

Claims 1-2, 4-6, 8-9, 14-18, 20, 22-23, 25-26, are rejected under 35 U.S.C. 103(a) as being unpatentable over Braunlich et al., EP 0 731 099 B1.

Applicant claims compounds of formula (I), composition and method of use for treating or preventing a hyperproliferative disorder. In the compound, X is O or S; R1 is alkyl, C(O)(C1-6)alkyl or benzyl; R2 is alkyl, optionally substituted heterocycle; R3 is H, alkoxy, or alkyl; R4 is alkoxy, C(O)RD, RD is H, alkyl, alkoxy or cycloalkyl; R5 and R6 are H, alkoxy or halogen.

*Determination of the scope and content of the prior art (MPEP ∋2141.01*

McKinnon et al., teach the checked compound of formula (I) in the attached abstract, wherein X is S; R1 is benzyl; R2 is Het.; R3-R6 are H.

Boeshagen et al., teach the checked compound of formula (I) in the attached abstract, wherein X is S; R1 is alkyl; R2 is Het.; R3-R6 are H.

Harwalkar et al., teach the checked compounds of formula (I) in the attached abstract, wherein X is O; R1 is alkyl, acetyl, or benzyl; R2 is Het.; R3-R6 are H.

Osswald et al., teach the checked compound of formula (I) in the attached abstract, wherein X is O; R1 H; R2 is Het.; R3-R6 are H.

Radl et al., teach the checked compounds of formula (I) in the attached abstract, wherein X is O or S; R1 H; R2 is Het.; R3-R6 are H.

Braunlich et al., teach the compounds III-IV, VIII, XI-XIII, XXVI, XXVIII-XXXIII, XXXV-XLVIII, LI-LV, LVI-LIX, LXV-LXVII, LXIX, their compositions and method of use for treating various proliferative disorders. See Tables I-V, and paragraphs 0028 and 0029 on page 10. In the compounds X is O; R1 H, alky, or ketoalkyl; R2 is optionally substituted Het.; R3 is H or alkoxy; R4 is H, alkoxy or alkylester; R5 is H, alkoxy or halogen and R6 is H.

*Ascertainment of the difference between the prior art and the claims (MPEP ∋2141.02)*

The difference between the instant invention and that of McKinnon et al., Boeshagen et al., Harwalkar et al., Osswald et al., Radl et al., or Braunlich et al., is that alkyl is claimed at position R4 instead of H by McKinnon et al., Boeshagen et al., Harwalkar et al., Osswald et al., Radl et al., or Braunlich et al.

*Finding of prima facie obviousness--rational and motivation (MPEP ∋2142.2413)*

However, H and alkyl are art recognized equivalents. *In re Lincoln*, 53 USPQ 40 (CCPA, 1942); *In re Druey*, 319 F.2d 237, 138 USPQ 39 (CCPA, 1963); *In re Lohr*, 317 F.2d 388, 137 USPQ 548 (CCPA, 1963); *In re Hoehsema*, 399 F.2d 269, 158 USPQ 598 (CCPA, 1968); *In re Wood*, 582 F.2d 638, 199 USPQ 137 (CCPA, 1978); *In re Hoke*, 560 F.2d 436, 195 USPQ 148 (CCPA, 1977); *Ex parte Fauque*, 121 USPQ 425 (POBA, 1954); *Ex parte Henkel*, 130 USPQ 474, (POBA, 1960).

Therefore, the instant invention is prima facie obvious from the compounds of McKinnon et al., Boeshagen et al., Harwalkar et al., Osswald et al., Radl et al., or Braunlich et al. One of ordinary skill in the art would have known to replace alkyl with H at the time the instant invention was made. The motivation is from the knowing that H and alkyl are equivalents.

***Allowable Subject Matter***

Claims 7, 13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

TAOFIQ SOLOLA
PRIMARY EXAMINER

Group 1626

October 8, 2006